PATENT
Docket No. P-10998.00
(134.01930101)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellant(s):	SPARER et al.	Group Art Unit:	1618
Serial No.:	10/640,853	Examiner:	James William Rogers
Confirmation No.:	9178		
Filed:	August 13, 2003		
For:	ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS		

APPEAL BRIEF

Commissioner for Patents
Mail Stop Appeal Brief - Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This Brief is presented in support of the Appeal filed herewith, from the final rejection of claims 89, 91-104, 134-138, and 140-150 of the above-identified application under 37 C.F.R. §§1.113 and 1.191.

This Brief is being submitted as set forth in 37 C.F.R. §41.37. Please charge PTO Deposit Account No. 13-4895 in the amount of $ 0 to cover the Appeal Brief filing fee. Appellants previously paid $1520 in appeal fees in the present application ($500 on July 11, 2007; $510 on January 29, 2008; and $510 on March 28, 2008) without a final Board decision. From this, $540 was applied to the filing of a Notice of Appeal on September 27, 2010. Pursuant to M.P.E.P. §1204.01, Appellants submit that the previously paid appeal fees may be applied also to the $540 fee for filing the present Notice of Appeal. Thus, it is believed that no fee is due.

Please charge any additional fees or credit any over-payment to PTO Deposit Account No. 13-4895.

I. REAL PARTY IN INTEREST

The real party in interest of the above-identified patent application is the assignee, Medtronic, Inc., as evidenced by the assignment recorded at Reel 014508, Frame 0287 on August 13, 2003.

II. RELATED APPEALS AND INTERFERENCES

Appellants direct the Board's attention to U.S. Patent Application Serial Nos. 10/640,713, 10/640,823, 10/916,162, 10/640,714, 10/640,702, and 10/916,159. Although these applications are not technically related to the present application, Appellants wish to bring the appeals in each case to the Board's attention as potentially bearing on the Board's decision in the pending appeal.

III. STATUS OF CLAIMS

Claims 1-88 have been previously cancelled. Claims 90, 105-133, and 139 have been withdrawn from consideration. Claims 89, 91-104, 134-138, and 140-150 were finally rejected in the Office Action dated July 27, 2010.

Thus, claims 89-150 are pending. Claims 89, 91-104, 134-138, and 140-150 are the subject of this appeal (see Claims Appendix).

IV. STATUS OF AMENDMENTS

No claim amendments have been filed since issuance of the Office Action dated July 27, 2010 finally rejecting claims 89, 91-104, 134-138, and 140-150.

V. SUMMARY OF CLAIMED SUBJECT MATTER

Claim 89 recites a method of tuning the delivery of an active agent from an implantable medical device to a subject at a target diffusivity. (See, e.g., Appellants' Specification, page 8, lines 10-20, page 9, lines 3-5, page 18, lines 12-17, and page 26, line 29 to page 28, line 8.)

The method includes receiving an implantable medical device comprising an active agent delivery system, wherein the active agent delivery system comprises an active agent and a miscible polymer blend. (See, e.g., Appellants' Specification, page 8, lines 10-16 and page 33, line 25 to page 34, line 26.) The active agent delivery system is formed by a method including receiving a hydrophobic active agent having a molecular weight of no greater than about 1200 g/mol (see, e.g., Appellants' Specification, page 17, line 4 to page 18, line 7); receiving a first polymer (see, e.g., Appellants' Specification, page 9, lines 22-24); receiving a second polymer selected to be miscible with the first polymer to form a miscible polymer blend that controls the delivery of the active agent (see, e.g., Appellants' Specification, page 12, lines 14-17); wherein at least one polymer has an active agent diffusivity higher than the target diffusivity and at least one polymer has an active agent diffusivity lower than the target diffusivity (see, e.g., Appellants' Specification, page 27, lines 21-28); wherein each of the first polymer and the second miscible polymer has at least one solubility parameter, and the difference between at least one solubility parameter of each of the polymers is no greater than about 3 $J^{1/2}/cm^{3/2}$ (see, e.g., Appellants' Specification, page 18, line 28 to page 19, line 5); wherein the active agent has a solubility parameter and the difference between the solubility parameter of the active agent and at least one solubility parameter of at least one of the polymers is no greater than about 3 $J^{1/2}/cm^{3/2}$ (see, e.g., Appellants' Specification, page 18, line 28 to page 19, line 5); and further wherein each of the solubility parameters is independently determined by at least one method selected from measuring, obtaining the solubility parameter from a reference publication, taking an average of calculations performed using the Hoy Method and the Hoftyzer-van Krevelen Method, and

calculating by computer simulation (see, e.g., Appellants' Specification, page 19, lines 6-15); and combining the first and second polymers in amounts sufficient to form a miscible polymer blend that controls the delivery of the active agent over a period of time (see, e.g., Appellants' Specification, page 9, lines 3-9); wherein: the swellability of the miscible polymer blend is no greater than 10% by volume (see, e.g., Appellants' Specification, page 29, line 30 to page 30, line 2); and the molar average solubility parameter of the miscible polymer blend is no greater than 25 $J^{1/2}/cm^{3/2}$ (see, e.g., Appellants' Specification, page 26, lines 1-24); and further wherein: the miscible polymer blend comprises at least one hydrophobic cellulose derivative (see, e.g., Appellants' Amendment and Response dated November 1, 2006, page 2, line 3 to page 3, line 4) and at least one miscible polyvinyl homopolymer or copolymer selected from the group consisting of a polyvinyl alkylate homopolymer or copolymer, a polyvinyl alkyl ether homopolymer or copolymer, a polyvinyl acetal homopolymer or copolymer, and combinations thereof (see, e.g., Appellants' Amendment and Response dated November 1, 2006, page 3, lines 5-11); or the miscible polymer blend comprises a polyurethane (see, e.g., Appellants' Amendment and Response dated November 1, 2006, page 4, lines 14-21) and a second miscible polymer that is not a hydrophobic cellulose ester; wherein the second miscible polymer is selected from the group consisting of a polycarbonate, a polysulfone, a polyurethane, a polyphenylene oxide, a polyimide, a polyamide, a polyester, a polyether, a polyketone, a polyepoxide, a styrene-acrylonitrile copolymer, a poly(vinyl ester), a poly(vinyl ether), a polyacrylate, a poly(methyl acrylate), a polymethacrylate, a poly(methyl methacrylate), and combinations thereof (see, e.g., Appellants' Amendment and Response dated November 1, 2006, page 6, lines 16-22); or the miscible polymer blend comprises a poly(ethylene-co-(meth)acrylate) (see, e.g., Appellants' Amendment and Response dated November 1, 2006, page 8, lines 9-15) and a second miscible polymer not including poly(ethylene vinyl acetate); wherein the second miscible polymer is selected from the group consisting of a poly(vinyl alkylate) homopolymer or

copolymer, a poly(vinyl alkyl ether) homopolymer or copolymer, a poly(vinyl acetal) homopolymer or copolymer, a poly(alkyl and/or aryl methacrylate) homopolymer or copolymer, a poly(alkyl and/or aryl acrylate) homopolymer or copolymer, and combinations thereof (see, e.g., Appellants' Amendment and Response dated November 1, 2006, page 8, line 24 to page 9, line 13).

The method also includes contacting the implantable medical device comprising the active agent delivery system with a bodily fluid, organ, or tissue of a subject to deliver the active agent over a period of time, which is not controlled by porosity in the miscible polymer blend. (See, e.g., Appellants' Specification, page 33, line 25 to page 34, line 26.)

Claim 134 recites a method of tuning the delivery of an active agent from an implantable medical device to a subject at a target diffusivity. (See, e.g., Appellants' Specification, page 8, lines 10-20, page 9, lines 3-5, page 18, lines 12-17, and page 26, line 29 to page 28, line 8.)

The method includes receiving an implantable medical device comprising an active agent delivery system, wherein the active agent delivery system comprises an active agent and a miscible polymer blend. (See, e.g., Appellants' Specification, page 8, lines 10-16 and page 33, line 25 to page 34, line 26.) The active agent delivery system is formed by a method including receiving a hydrophilic active agent having a molecular weight of greater than about 1200 g/mol (see, e.g., Appellants' Specification, page 17, line 4 to page 18, line 7); receiving a first polymer (see, e.g., Appellants' Specification, page 9, lines 22-24); receiving a second polymer selected to be miscible with the first polymer to form a miscible polymer blend that controls the delivery of the active agent (see, e.g., Appellants' Specification, page 12, lines 14-17); wherein at least one polymer has an active agent diffusivity higher than the target diffusivity and at least one polymer has an active agent diffusivity lower than the target diffusivity (see, e.g., Appellants' Specification, page 27, lines 21-28); wherein each of the first polymer and the second miscible

polymer has at least one solubility parameter, and the difference between at least one solubility parameter of each of the polymers is no greater than about 3 $J^{1/2}/cm^{3/2}$ (see, e.g., Appellants' Specification, page 18, line 28 to page 19, line 5); wherein the active agent has a solubility parameter and the difference between the solubility parameter of the active agent and at least one solubility parameter of at least one of the polymers is no greater than about 3 $J^{1/2}/cm^{3/2}$ (see, e.g., Appellants' Specification, page 18, line 28 to page 19, line 5); and further wherein each of the solubility parameters is independently determined by at least one method selected from measuring, obtaining the solubility parameter from a reference publication, taking an average of calculations performed using the Hoy Method and the Hoftyzer-van Krevelen Method, and calculating by computer simulation (see, e.g., Appellants' Specification, page 19, lines 6-15); and combining the first and second polymers in amounts sufficient to form a miscible polymer blend that controls the delivery of the active agent over a period of time (see, e.g., Appellants' Specification, page 9, lines 3-9); wherein: the swellability of the miscible polymer blend is greater than 10% by volume (see, e.g., Appellants' Specification, page 32, lines 5-10); and the molar average solubility parameter of the miscible polymer blend is greater than 25 $J^{1/2}/cm^{3/2}$ (see, e.g., Appellants' Specification, page 32, lines 5-10); and further wherein: the miscible polymer blend comprises at least one hydrophilic polymer (see, e.g., Appellants' Amendment and Response dated November 1, 2006, page 11, line 24 to page 12, line 3) and a second miscible polymer that is hydrophilic or hydrophobic (see, e.g., Appellants' Amendment and Response dated November 1, 2006, page 12, lines 4-8); wherein the hydrophilic polymer is selected from the group consisting of a polyurethane, a polyvinyl alcohol, a poly(alkylene ether), a polyvinyl pyridine, a polyvinyl pyrrolidone, a polyacrylonitrile, a polyacrylamide, a polyvinyl pyrrolidone/polyvinyl acetate copolymer, a sulfonated polystyrene, a polyvinyl pyrrolidone/polystyrene copolymer, a polysaccharide, a xanthan, a hydrophilic cellulose derivative, a hyaluronic acid, a hydrophilic polyacrylate, a hydrophilic polymethacrylate, a DNA

or analog thereof, an RNA or analog thereof, heparin, a chitosan, a polyethylene imine, a polyacrylamide, an amine-containing polymer, and combinations thereof (see, e.g., Appellants' Amendment and Response dated November 1, 2006, page 13, line 14 to page 14, line 2); and the hydrophobic polymer is selected from the group consisting of a polyurethane, a polycarbonate, a polysulfone, a polyphenylene oxide, a polyimide, a polyamide, a polyester, a polyether, a polyketone, a polyepoxide, a styrene-acrylonitrile copolymer, a polyvinyl alkylate, a polyvinyl alkyl ether, a polyvinyl acetal, a hydrophobic cellulose derivative, and combinations thereof (see, e.g., Appellants' Amendment and Response dated November 1, 2006, page 14, lines 14-23).

The method also includes contacting the implantable medical device comprising the active agent delivery system with a bodily fluid, organ, or tissue of a subject to deliver the active agent over a period of time, which is not controlled by porosity in the miscible polymer blend. (See, e.g., Appellants' Specification, page 33, line 25 to page 34, line 26.)

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

A. Claims 89, 91, 93-104, 134-138, 140, 141, and 143-150 stand rejected under 35 U.S.C. §102(b) as being anticipated by Hossainy et al. (U.S. Patent No. 6,153,252).

B. Claims 89, 91, 93-104, 134-138, 140, 141, and 143-150 stand rejected under 35 U.S.C. §102(b) as being anticipated by Whitbourne et al. (U.S. Patent No. 6,110,483).

C. Claims 89, 91, 93-104, 134-138, 140, 141, and 143-150 stand rejected under 35 U.S.C. §102(e) as being anticipated by Sirhan et al. (U.S. 2002/0082679 A1).

D. Claims 89, 91-97, 99, 101-103, 134-138, 140-143, 145, and 147-150 stand rejected under 35 U.S.C. §102(e) as being anticipated by Atala (U.S. Patent No. 6,576,019).

E. Claims 89, 91, 93-104, 134-138, 140, 141, and 143-150 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Sirhan et al. (U.S. 2002/0082679 A1) in view of Van Krevelen (Properties of Polymers, 3rd ed., Chapter 7, 189-225).

F. Claims 89, 91, 93-104, 134-138, 140, 141, and 143-150 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Sirhan et al. (U.S. 2002/0082679 A1), in view of Coleman et al. (Specific Interactions and the Miscibility of Polymer Blends, Ch. 2: A Practical Guide to Polymer Miscibility, 1991; 49-156).

G. Claims 89, 91, 93-104, 134-138, 140, 141, and 143-150 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Hossainy et al. (U.S. Patent No. 6,153,252) in view of Van Krevelen (Properties of Polymers, 3rd ed., Chapter 7, 189-225).

H. Claims 89, 91, 93-104, 134-138, 140, 141, and 143-150 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Hossainy et al. (U.S. Patent No. 6,153,252) in view of Coleman et al. (Specific Interactions and the Miscibility of Polymer Blends, Ch. 2: A Practical Guide to Polymer Miscibility, 1991; 49-156).

I. Claims 89, 91, 93-104, 134-138, 140, 141, and 143-150 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Whitbourne et al. (U.S. Patent No. 6,110,483), in view of Van Krevelen (Properties of Polymers, 3rd ed., Chapter 7, 189-225).

J. Claims 89, 91, 93-104, 134-138, 140, 141, and 143-150 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Whitbourne et al. (U.S. Patent No. 6,110,483), in view of Coleman et al. (Specific Interactions and the Miscibility of Polymer Blends, Ch. 2: A Practical Guide to Polymer Miscibility, 1991; 49-156).

K. Claims 89, 91-97, 99, 101-103, 134-138, 140-143, 145, and 147-150 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Atala (U.S. Patent No. 6,576,019) in view of Van Krevelen (Properties of Polymers, 3rd ed., Chapter 7, 189-225).

L. Claims 89, 91-97, 99, 101-103, 134-138, 140-143, 145, and 147-150 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Atala (U.S. Patent No. 6,576,019) in view of Coleman et al. (Specific Interactions and the Miscibility of Polymer Blends, Ch. 2: A Practical Guide to Polymer Miscibility, 1991; 49-156).

VII. ARGUMENT

A. Claims 89, 91, 93-104, 134-138, 140, 141, and 143-150 are not anticipated under 35 U.S.C. §102(b) by Hossainy et al. (U.S. Patent No. 6,153,252).

There is no teaching or suggestion in Hossainy et al. of a method of tuning the delivery of an active agent from an implantable medical device to a subject using a miscible polymer blend, with the recited relationships of solubility parameters between the polymers and active agent, over a period of time, which is not controlled by porosity in the miscible polymer blend. In particular, each of the independent claims explicitly recites a combination of at least the following eight relationships, parameters, and functions that cannot be found in Hossainy et al.: (1) miscibility of the first and second polymers, (2) diffusivity of each polymer relative to each other and a target diffusivity, (3) a specific upper difference in solubility parameter between the first and second polymers, (4) a specific upper difference in solubility parameter between the active agent and either the first or second polymer, (5) a specific upper swellability of the polymer blend, (6) a specific upper molar average solubility parameter of the polymer blend, (7) specific combinations of polymer chemical classes, and (8) the miscible polymer blend controlling the delivery of the active agent, which is not controlled by porosity in the miscible polymer blend. All of these specifically recited relationships, parameters, and functions further define a subset of combinations of polymers and active agents more specifically than in Hossainy et al. Furthermore, with respect to dependent claims 102 and 148, there is no teaching or suggestion in Hossainy et al. that delivery of the active agent occurs predominantly under permeation control.

M.P.E.P. §2131 states, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Also, as discussed in *Net MoneyIN, Inc. v. Verisign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008), because the hallmark of anticipation is prior invention, the prior art reference—in order to

anticipate under 35 U.S.C. §102—must not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements "arranged as in the claim" (citing *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983)). That is, the Federal Circuit clarified that ". . .[P]recedent informs that the 'arranged as in the claim' requirement applies to all claims and refers to the need for an anticipatory reference to show all of the limitations of the claims arranged or combined in the same way as recited in the claims, not merely in a particular order. The test is thus more accurately understood to mean 'arranged or combined in the same way as in the claim.'" *Net MoneyIN*, 545 F.3d at 1370.

The Federal Circuit thus held that unless a reference discloses within the four corners of the document not only all of the limitations claimed but also all of the limitations arranged or combined in the same way as recited in the claim, it cannot be said to prove prior invention of the thing claimed and, thus, cannot anticipate under 35 U.S.C. §102. Accordingly, any rejection of the presently pending claims under 35 U.S.C. §102 must fail.

Hossainy et al. teach processes for coating stents. Although Hossainy et al. teach certain types of polymers that encompass at least some of the polymers from which polymers of Appellants' miscible polymer blend may be selected, Hossainy et al. list over 30 classes of polymers that encompass innumerable species of polymers (arguably thousands if not hundreds of thousands or more) at columns 4 and 5. This list includes references to a handbook (The Handbook of Biodegradable Polymers), an encyclopedia (The Encyclopedia of Polymer Science), journal articles (in Polymer Preprints and Journal of Biomaterials Research), and patents (16 patents).

Hossainy et al. fail to expressly or inherently set forth the specific polymer combinations and active agents recited in the claims. Again, each of the independent claims explicitly recites a combination of at least the following eight relationships, parameters, and functions that cannot be found in Hossainy et al.: (1) miscibility of the first and second polymers, (2) diffusivity of each

polymer relative to each other and a target diffusivity, (3) a specific upper difference in solubility parameter between the first and second polymers, (4) a specific upper difference in solubility parameter between the active agent and either the first or second polymer, (5) a specific upper swellability of the polymer blend, (6) a specific upper molar average solubility parameter of the polymer blend, (7) specific combinations of polymer chemical classes, and (8) the miscible polymer blend controlling the delivery of the active agent, which is not controlled by porosity in the miscible polymer blend. For example, although Hossainy et al. may teach some of the same classes of polymers from which the first and second polymer may be selected, Hossainy et al. fail to teach the specific individual polymers from among the classes listed that one should select so that the second polymer will be miscible with the first polymer and possess the recited difference in solubility parameter with respect to the first polymer. That is, Hossainy et al. fail to teach, expressly or inherently, the step of receiving the second polymer selected to be miscible with the first polymer and to possess a solubility parameter that differs from the solubility parameter of the first polymer by no greater than 3 $J^{1/2}/cm^{3/2}$. Furthermore, Hossainy et al. fail to teach, expressly or inherently, the relationship between the active agent and the polymers of the miscible polymer blend as recited in each of Appellants' independent claims. Thus, Hossainy et al. cannot anticipate Appellants' claims.

Appellants note that the Examiner alleged at page 10 of the Office Action dated July 27, 2010 that "[i]t appears as though applicants are attempting to claim a well known and established scientific principle," "[e]ssentially applicants believe that the inventiveness of their claimed invention stems from the fact that like dissolves like," and "the examiner will not give patentable weight to claims directed to the well known scientific principle of mentally selecting ingredients that will be soluble with each other." Appellants earnestly disagree with all of these allegations. Rather, as discussed herein above, Appellants have claimed methods that recite, among other

things, a specific subset of combinations of polymers and active agents according to specifically recited relationships, parameters, and functions.

Review and reversal by the Board of the 35 U.S.C. §102 rejection based on Hossainy et al. are respectfully requested.

B. Claims 89, 91, 93-104, 134-138, 140, 141, and 143-150 are not anticipated under 35 U.S.C. §102(b) by Whitbourne et al. (U.S. Patent No. 6,110,483).

There is no teaching or suggestion in Whitbourne et al. of a method of tuning the delivery of an active agent from an implantable medical device to a subject using a miscible polymer blend, with the recited relationships of solubility parameters between the polymers and active agent, over a period of time, which is not controlled by porosity in the miscible polymer blend. In particular, each of the independent claims explicitly recites a combination of at least the following eight relationships, parameters, and functions that cannot be found in Whitbourne et al.: (1) miscibility of the first and second polymers, (2) diffusivity of each polymer relative to each other and a target diffusivity, (3) a specific upper difference in solubility parameter between the first and second polymers, (4) a specific upper difference in solubility parameter between the active agent and either the first or second polymer, (5) a specific upper swellability of the polymer blend, (6) a specific upper molar average solubility parameter of the polymer blend, (7) specific combinations of polymer chemical classes, and (8) the miscible polymer blend controlling the delivery of the active agent, which is not controlled by porosity in the miscible polymer blend. All of these specifically recited relationships, parameters, and functions further define a subset of combinations of polymers and active agents more specifically than in Whitbourne et al. Furthermore, with respect to dependent claims 102 and 148, there is no teaching or suggestion in Whitbourne et al. that delivery of the active agent occurs predominantly under permeation control.

M.P.E.P. §2131 states, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Also, as discussed in *Net MoneyIN, Inc. v. Verisign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008), because the hallmark of anticipation is prior invention, the prior art reference—in order to anticipate under 35 U.S.C. §102—must not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements "arranged as in the claim" (citing *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983)). That is, the Federal Circuit clarified that ". . .[P]recedent informs that the 'arranged as in the claim' requirement applies to all claims and refers to the need for an anticipatory reference to show all of the limitations of the claims arranged or combined in the same way as recited in the claims, not merely in a particular order. The test is thus more accurately understood to mean 'arranged or combined in the same way as in the claim.'" *Net MoneyIN*, 545 F.3d at 1370.

The Federal Circuit thus held that unless a reference discloses within the four corners of the document not only all of the limitations claimed but also all of the limitations arranged or combined in the same way as recited in the claim, it cannot be said to prove prior invention of the thing claimed and, thus, cannot anticipate under 35 U.S.C. §102. Accordingly, any rejection of the presently pending claims under 35 U.S.C. §102 must fail.

Whitbourne et al. teach polymer coatings for medical devices. Whitbourne et al. teach more than a dozen classes of polymers in columns 5 and 6, which, as in Hossainy et al. (discussed herein above), include innumerable species of polymers. Whitbourne et al. also includes polymers discussed in two encyclopedias (Concise Encyclopedia of Polymer Science and Engineering, and Kirk-Othmer Concise Encyclopedia of Chemical Technology).

Whitbourne et al. fail to expressly or inherently set forth the specific polymer combinations recited in the claims. The mere listing in Whitbourne et al. of general classes of polymers that includes classes similarly identified in Appellants' specification is insufficient to

necessarily—i.e., inherently—teach the specific subpopulations of combinations recited in Appellants' claims. Whitbourne et al. fail to teach the specific individual polymers from among the classes listed in the Office Action that one should select so that the second polymer will be miscible with the first polymer and possess the recited difference in solubility parameter with respect to the first polymer.

Also, Whitbourne et al., like Hossainy et al. (discussed herein above), fail to teach, expressly or inherently, the step of receiving the second polymer selected to be miscible with the first polymer and to possess a solubility parameter that differs from the solubility parameter of the first polymer by no greater than 3 $J^{1/2}/cm^{3/2}$. Again, each of the independent claims explicitly recites a combination of at least the following eight relationships, parameters, and functions that cannot be found in Whitbourne et al.: (1) miscibility of the first and second polymers, (2) diffusivity of each polymer relative to each other and a target diffusivity, (3) a specific upper difference in solubility parameter between the first and second polymers, (4) a specific upper difference in solubility parameter between the active agent and either the first or second polymer, (5) a specific upper swellability of the polymer blend, (6) a specific upper molar average solubility parameter of the polymer blend, (7) specific combinations of polymer chemical classes, and (8) the miscible polymer blend controlling the delivery of the active agent, which is not controlled by porosity in the miscible polymer blend. Furthermore, Whitbourne et al. fail to teach, expressly or inherently, the relationship between the active agent and the polymers of the miscible polymer blend as recited in each of Appellants' independent claims. Thus, Whitbourne et al. cannot anticipate Appellants' claims.

Appellants note that the Examiner alleged at page 10 of the Office Action dated July 27, 2010 that "[i]t appears as though applicants are attempting to claim a well known and established scientific principle," "[e]ssentially applicants believe that the inventiveness of their claimed invention stems from the fact that like dissolves like," and "the examiner will not give patentable

weight to claims directed to the well known scientific principle of mentally selecting ingredients that will be soluble with each other." Appellants earnestly disagree with all of these allegations. Rather, as discussed herein above, Appellants have claimed methods that recite, among other things, a specific subset of combinations of polymers and active agents according to specifically recited relationships, parameters, and functions.

Review and reversal by the Board of the 35 U.S.C. §102 rejection based on Whitbourne et al. are respectfully requested.

C. Claims 89, 91, 93-104, 134-138, 140, 141, and 143-150 are not anticipated under 35 U.S.C. §102(e) by Sirhan et al. (U.S. 2002/0082679 A1).

There is no teaching or suggestion in Sirhan et al. of a method of tuning the delivery of an active agent from an implantable medical device to a subject using a miscible polymer blend, with the recited relationships of solubility parameters between the polymers and active agent, over a period of time, which is not controlled by porosity in the miscible polymer blend. In particular, each of the independent claims explicitly recites a combination of at least the following eight relationships, parameters, and functions that cannot be found in Sirhan et al.: (1) miscibility of the first and second polymers, (2) diffusivity of each polymer relative to each other and a target diffusivity, (3) a specific upper difference in solubility parameter between the first and second polymers, (4) a specific upper difference in solubility parameter between the active agent and either the first or second polymer, (5) a specific upper swellability of the polymer blend, (6) a specific upper molar average solubility parameter of the polymer blend, (7) specific combinations of polymer chemical classes, and (8) the miscible polymer blend controlling the delivery of the active agent, which is not controlled by porosity in the miscible polymer blend. All of these specifically recited relationships, parameters, and functions further define a subset of combinations of polymers and active agents more specifically than in Sirhan et

al. Furthermore, with respect to dependent claims 102 and 148, there is no teaching or suggestion in Sirhan et al. that delivery of the active agent occurs predominantly under permeation control.

M.P.E.P. §2131 states, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Also, as discussed in *Net MoneyIN, Inc. v. Verisign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008), because the hallmark of anticipation is prior invention, the prior art reference—in order to anticipate under 35 U.S.C. §102—must not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements "arranged as in the claim" (citing *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983)). That is, the Federal Circuit clarified that ". . .[P]recedent informs that the 'arranged as in the claim' requirement applies to all claims and refers to the need for an anticipatory reference to show all of the limitations of the claims arranged or combined in the same way as recited in the claims, not merely in a particular order. The test is thus more accurately understood to mean 'arranged or combined in the same way as in the claim.'" *Net MoneyIN*, 545 F.3d at 1370.

The Federal Circuit thus held that unless a reference discloses within the four corners of the document not only all of the limitations claimed but also all of the limitations arranged or combined in the same way as recited in the claim, it cannot be said to prove prior invention of the thing claimed and, thus, cannot anticipate under 35 U.S.C. §102. Accordingly, any rejection of the presently pending claims under 35 U.S.C. §102 must fail.

Sirhan et al. teach luminal prosthetic devices that allow for controlled release of a therapeutic agent (Abstract). More than a dozen classes of suitable polymers are listed in paragraphs [0119] and [0120], including "mixtures, copolymers, and combinations thereof" for each set of polymers. Sirhan et al. describe certain classes and/or types of polymers that are identified in Appellants' specification as classes and/or types from which polymers may be

selected to form the particular subpopulation of miscible polymer blends recited in Appellants' claims.

Sirhan et al. fail to expressly or inherently set forth the specific polymer combinations and active agents recited in the claims. Again, each of the independent claims explicitly recites a combination of at least the following eight relationships, parameters, and functions that cannot be found in Sirhan et al.: (1) miscibility of the first and second polymers, (2) diffusivity of each polymer relative to each other and a target diffusivity, (3) a specific upper difference in solubility parameter between the first and second polymers, (4) a specific upper difference in solubility parameter between the active agent and either the first or second polymer, (5) a specific upper swellability of the polymer blend, (6) a specific upper molar average solubility parameter of the polymer blend, (7) specific combinations of polymer chemical classes, and (8) the miscible polymer blend controlling the delivery of the active agent, which is not controlled by porosity in the miscible polymer blend. Also, Sirhan et al. fail to teach, expressly or inherently, the step of receiving the second polymer selected to be miscible with the first polymer and to possess a solubility parameter that differs from the solubility parameter of the first polymer by no greater than 3 $J^{1/2}/cm^{3/2}$. Furthermore, Sirhan et al. fail to teach, expressly or inherently, the relationship between the active agent and the polymers of the miscible polymer blend as recited in each of Appellants' independent claims. Thus, Sirhan et al. cannot anticipate Appellants' claims. Appellants therefore respectfully request notification to this effect.

Appellants note that the Examiner alleged at page 10 of the Office Action dated July 27, 2010 that "[i]t appears as though applicants are attempting to claim a well known and established scientific principle," "[e]ssentially applicants believe that the inventiveness of their claimed invention stems from the fact that like dissolves like," and "the examiner will not give patentable weight to claims directed to the well known scientific principle of mentally selecting ingredients that will be soluble with each other." Appellants earnestly disagree with all of these allegations.

Rather, as discussed herein above, Appellants have claimed methods that recite, among other things, a specific subset of combinations of polymers and active agents according to specifically recited relationships, parameters, and functions.

Review and reversal by the Board of the 35 U.S.C. §102 rejection based on Sirhan et al. are respectfully requested.

D. Claims 89, 91-97, 99, 101-103, 134-138, 140-143, 145, and 147-150 are not anticipated under 35 U.S.C. §102(e) by Atala (U.S. Patent No. 6,576,019).

There is no teaching or suggestion in Atala of a method of tuning the delivery of an active agent from an implantable medical device to a subject using a miscible polymer blend, with the recited relationships of solubility parameters between the polymers and active agent, over a period of time, which is not controlled by porosity in the miscible polymer blend. In particular, each of the independent claims explicitly recites a combination of at least the following eight relationships, parameters, and functions that cannot be found in Atala: (1) miscibility of the first and second polymers, (2) diffusivity of each polymer relative to each other and a target diffusivity, (3) a specific upper difference in solubility parameter between the first and second polymers, (4) a specific upper difference in solubility parameter between the active agent and either the first or second polymer, (5) a specific upper swellability of the polymer blend, (6) a specific upper molar average solubility parameter of the polymer blend, (7) specific combinations of polymer chemical classes, and (8) the miscible polymer blend controlling the delivery of the active agent, which is not controlled by porosity in the miscible polymer blend. All of these specifically recited relationships, parameters, and functions further define a subset of combinations of polymers and active agents more specifically than in Atala. Furthermore, with respect to dependent claims 102 and 148, there is no teaching or suggestion in Atala that delivery of the active agent occurs predominantly under permeation control.

M.P.E.P. §2131 states, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Also, as discussed in *Net MoneyIN, Inc. v. Verisign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008), because the hallmark of anticipation is prior invention, the prior art reference—in order to anticipate under 35 U.S.C. §102—must not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements "arranged as in the claim" (citing *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983)). That is, the Federal Circuit clarified that ". . .[P]recedent informs that the 'arranged as in the claim' requirement applies to all claims and refers to the need for an anticipatory reference to show all of the limitations of the claims arranged or combined in the same way as recited in the claims, not merely in a particular order. The test is thus more accurately understood to mean 'arranged or combined in the same way as in the claim.'" *Net MoneyIN*, 545 F.3d at 1370.

The Federal Circuit thus held that unless a reference discloses within the four corners of the document not only all of the limitations claimed but also all of the limitations arranged or combined in the same way as recited in the claim, it cannot be said to prove prior invention of the thing claimed and, thus, cannot anticipate under 35 U.S.C. §102. Accordingly, any rejection of the presently pending claims under 35 U.S.C. §102 must fail.

Atala teaches bladder reconstruction. Although Atala teaches certain types of polymers that encompass at least some of the polymers from which polymers of Appellants' miscible polymer blend may be selected, Atala fails to expressly or inherently set forth the specific polymer combinations and active agents recited in the claims with the recited differences in solubility parameters. Again, each of the independent claims explicitly recites a combination of at least the following eight relationships, parameters, and functions that cannot be found in Atala: (1) miscibility of the first and second polymers, (2) diffusivity of each polymer relative to each other and a target diffusivity, (3) a specific upper difference in solubility parameter between the

first and second polymers, (4) a specific upper difference in solubility parameter between the active agent and either the first or second polymer, (5) a specific upper swellability of the polymer blend, (6) a specific upper molar average solubility parameter of the polymer blend, (7) specific combinations of polymer chemical classes, and (8) the miscible polymer blend controlling the delivery of the active agent, which is not controlled by porosity in the miscible polymer blend. That is, Atala fails to teach, expressly or inherently, the step of receiving the second polymer selected to be miscible with the first polymer and to possess a solubility parameter that differs from the solubility parameter of the first polymer by no greater than 3 $J^{1/2}/cm^{3/2}$. Furthermore, Atala fails to teach, expressly or inherently, the relationship between the active agent and the polymers of the miscible polymer blend as recited in each of Appellants' independent claims. Thus, Atala cannot anticipate Appellants' claims. Appellants therefore respectfully request notification to this effect.

Appellants note that the Examiner alleged at page 10 of the Office Action dated July 27, 2010 that "[i]t appears as though applicants are attempting to claim a well known and established scientific principle," "[e]ssentially applicants believe that the inventiveness of their claimed invention stems from the fact that like dissolves like," and "the examiner will not give patentable weight to claims directed to the well known scientific principle of mentally selecting ingredients that will be soluble with each other." Appellants earnestly disagree with all of these allegations. Rather, as discussed herein above, Appellants have claimed methods that recite, among other things, a specific subset of combinations of polymers and active agents according to specifically recited relationships, parameters, and functions.

Review and reversal by the Board of the 35 U.S.C. §102 rejection based on Atala are respectfully requested.

E. Claims 89, 91, 93-104, 134-138, 140, 141, and 143-150 are not unpatentable under 35 U.S.C. §103(a) over Sirhan et al. (U.S. 2002/0082679 A1) in view of Van Krevelen (Properties of Polymers, 3rd ed., Chapter 7, 189-225).

There is no teaching or suggestion in each cited document of a method of tuning the delivery of an active agent from an implantable medical device to a subject using a miscible polymer blend, with the recited relationships of solubility parameters between the polymers and active agent, over a period of time, which is not controlled by porosity in the miscible polymer blend. In particular, each of the independent claims explicitly recites a combination of at least the following eight relationships, parameters, and functions that cannot be found in the cited combination of documents: (1) miscibility of the first and second polymers, (2) diffusivity of each polymer relative to each other and a target diffusivity, (3) a specific upper difference in solubility parameter between the first and second polymers, (4) a specific upper difference in solubility parameter between the active agent and either the first or second polymer, (5) a specific upper swellability of the polymer blend, (6) a specific upper molar average solubility parameter of the polymer blend, (7) specific combinations of polymer chemical classes, and (8) the miscible polymer blend controlling the delivery of the active agent, which is not controlled by porosity in the miscible polymer blend. All of these specifically recited relationships, parameters, and functions further define a subset of combinations of polymers and active agents more specifically than in the cited combination of documents. Furthermore, with respect to dependent claims 102 and 148, there is no teaching or suggestion in the cited combination of documents that delivery of the active agent occurs predominantly under permeation control.

Appellants' system includes polymers that are miscible, focusing on a solubility parameter difference of no greater than about 3 $J^{1/2}/cm^{3/2}$. On this point of miscibility between polymers and tuning the release rates of active agents, the Examiner's attention is directed to Lyu et al., Journal of Controlled Release, 102, 679-687 (2005), in which tunable diffusion of an

active agent (dexamethasone) was achieved using a miscible polymer blend, but not with an immiscible polymer blend. See, for example, Figure 9.

Once again, the relevant disclosure of Sirhan et al. for analysis of the rejections is this: Sirhan et al. identify a vast number of individual polymer species. Furthermore, the document cited as a secondary reference (Van Krevelen) does not provide that which is missing from Sirhan et al. Van Krevelen merely teaches general theories about solubility parameters and predicting miscibility. Van Krevelen does not cure the deficiencies of Sirhan et al. or provide sufficient teaching or suggestion to select the combination of components recited in Appellants' claims, especially with respect to the identification of the specific combinations of polymers and active agents according to the recited combination of at least eight relationships, parameters, and functions enumerated herein above.

Appellants submit that while the cited combination of documents describes classes of polymers that encompass at least some of the polymers from which polymers used to form the miscible polymer blends in Appellants' claims may be selected, they neither teach nor suggest the selection criteria for the recited combinations of polymers and active agents. The cited combination of documents provide no blaze marks that would direct one skilled in the art to select polymers and active agents based on their miscibility and/or the recited differences in solubility parameter.

At page 5 of the Office Action dated July 27, 2010, the Examiner acknowledged that Appellants "have provided enough written description and showed enablement since the field of polymer blends is well known" and that "there are currently no 112 1st paragraph rejections over the breadth of the claims." The Examiner alleged that "[Appellants] argue, contradictory [*sic*], that a prior art reference which is similar to their claimed invention in that it also describes numerous types of polymer blends, does not disclose their claimed blend just because numerous combinations are possible." *Id.* at 5-6 (emphasis added). Appellants earnestly disagree that the

scope of the cited combination of documents is similar to the scope of the present claims. The materials recited in the present claims are described by chemistry (e.g., specific polymer chemical classes), physical properties (e.g., miscibility, relative diffusivities, difference in solubility parameters between polymers, difference in solubility parameters between the active agent and either the first or second polymer, swellability of the blend, molar average solubility parameter of the blend), and function (e.g., polymer blend controlling delivery of the active agent, which is not controlled by porosity in the polymer blend), which makes the number of combinations much smaller than that disclosed in the cited combination of documents.

The subsets of polymer and active agent combinations to which Appellants' claims are drawn is small and specific in relation to all of the possible combinations encompassed by the disclosures of the cited combination of documents and is not disclosed in the cited combination of documents. Moreover, the cited combination of documents provide no teaching or suggestion that would direct one skilled in the art to Appellants' claimed subset of polymer and active agent combinations from among the innumerable combinations described.

Appellants' position is supported by the decision of the Federal Circuit in *In re Baird*, 29 USPQ2d 1550 (1994), and, after *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007), the rationale used by the Federal Circuit in *In re Baird* was reiterated in *Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories Inc.*, 86 USPQ2d 1196 (Fed. Cir. 2008). The Federal Circuit reiterated that a claim cannot be rendered obvious by a prior disclosure that includes several unpredictable alternatives without some guidance to select features recited in the claim. The Federal Circuit contrasted a situation as presented in *KSR* (e.g., "a situation with a finite, and in the context of the art, small or easily traversed, number of options" 86 USPQ2d at 1201) with situations in which the path to the claimed subject matter is less direct. The Federal Circuit rejected the argument, based on language from *KSR*, that claims to a new drug were obvious in light of "a finite number of identified, predictable solutions." *Id.* The Federal Circuit

noted that one skilled in the art, even if provided with a general class of compound from which to start, would not necessarily have chosen the starting compound selected by the patentee. *Id.*

In the present application, the combined teachings of the suggested combination of documents describe innumerable polymer species, but provide no guidance to select polymers and an active agent in relation to one another, based on the at least eight criteria recited in Appellants' claims.

Appellants' position is further supported by a recent decision of the Federal Circuit. The Federal Circuit revisited the issue of the alleged obviousness of claimed subject matter in view of a generic disclosure that encompasses at least a portion of the claimed subject matter in *Süd-Chemie, Inc. v. Multisorb Technologies, Inc.*, 89 USPQ2d 1768 (2009). *Süd-Chemie, Inc.* involved a patent directed to a desiccant container made from a water-vapor-permeable, multilayered packaging material that included "compatible" polymeric materials, as the term "compatible" is defined in the specification of Süd-Chemie's patent. *Id.* at 1770. The patent was asserted against an alleged infringer, Multisorb, who argued that Süd-Chemie's patent was invalid as obvious over an earlier patent to Komatsu. The district court found that the polymeric materials in the Komatsu patent encompassed some of the "compatible" polymeric materials of Süd-Chemie's claims and granted summary judgment that Süd-Chemie's patent was invalid as obvious in view of the Komatsu patent. *Id.*

The Federal Circuit panel **REVERSED** the district court and critiqued the district court's analysis as follows:

> Finally, claim 1 of the '942 patent requires that the inner surfaces of the microporous and laminate films be "comprised of compatible polymeric materials." The district court concluded that Komatsu teaches the use of compatible films because "[t]he Komatsu patent suggests the employment of the same materials claimed by the '942 patent to be 'compatible polymeric materials.'" It is true that Komatsu discloses the same general classes of materials that are identified in the '942 patent. Thus, both patents state that

> the microporous and laminate films can be made from polyethylene, polypropylene, and other polyolefinic materials. *See* Komatsu, col. 2, ll. 19-21; col. 3, ll. 12-15; '942 patent, col. 5, ll. 12-15, 47-50. However, in concluding that Komatsu teaches the use of compatible polymeric materials, the district court failed to acknowledge that the specified classes of materials comprise a large number of substances with quite different properties, and that various combinations of those materials can be compatible or incompatible depending on how they are assembled in layers to form the container.

Id. at 1772 (emphases added).

The Federal Circuit held that the district court erred in ruling that Süd-Chemie's patent was invalid as obvious over the Komatsu patent, disagreeing with the district court "with regard to its conclusion that Komatsu teaches the same materials on the container's inner surface as those claimed in [Süd-Chemie's] patent." *Id.* at 1775.

The Federal Circuit's analysis in *Süd-Chemie* is directly applicable to the instant Application. The cited documents describe classes of polymers that may be blended, but those classes include innumerable species that have different properties, chief among those different properties are different solubility parameters. Thus, various combinations of members of the classes of polymers may possess the recited difference in solubility parameter or they may not, depending upon which members of the classes are selected.

Without guidance that directs one of ordinary skill in the art to miscible polymer blends and active agents having the recited differences in solubility parameter and the other specific relationships, the recitation of general classes of polymers and the general teaching that members of the classes may be combined does not render Appellants' claims obvious. The combinations of cited documents describe innumerable polymer species, but provide no guidance to select polymers and active agents in relation to one another and based on the criteria recited in Appellants' claims. Consequently, the obviousness analysis with respect to Appellants' claims is

similar to the analysis by the Federal Circuit in these post-*KSR* cases. Appellants respectfully submit that the presently pending claims are not obvious in view of the combinations of cited documents.

Appellants note that the Examiner alleged at page 10 of the Office Action dated July 27, 2010 that "[i]t appears as though applicants are attempting to claim a well known and established scientific principle," "[e]ssentially applicants believe that the inventiveness of their claimed invention stems from the fact that like dissolves like," and "the examiner will not give patentable weight to claims directed to the well known scientific principle of mentally selecting ingredients that will be soluble with each other." Appellants earnestly disagree with all of these allegations. Rather, as discussed herein above, Appellants have claimed methods that recite, among other things, a specific subset of combinations of polymers and active agents according to specifically recited relationships, parameters, and functions.

Review and reversal by the Board of the 35 U.S.C. §103 rejection based on Sirhan et al. in view of Van Krevelen are respectfully requested.

F. Claims 89, 91, 93-104, 134-138, 140, 141, and 143-150 are not unpatentable under 35 U.S.C. §103(a) over Sirhan et al. (U.S. 2002/0082679 A1), in view of Coleman et al. (Specific Interactions and the Miscibility of Polymer Blends, Ch. 2: A Practical Guide to Polymer Miscibility, 1991; 49-156).

There is no teaching or suggestion in each cited document of a method of tuning the delivery of an active agent from an implantable medical device to a subject using a miscible polymer blend, with the recited relationships of solubility parameters between the polymers and active agent, over a period of time, which is not controlled by porosity in the miscible polymer blend. In particular, each of the independent claims explicitly recites a combination of at least the following eight relationships, parameters, and functions that cannot be found in the cited

combination of documents: (1) miscibility of the first and second polymers, (2) diffusivity of each polymer relative to each other and a target diffusivity, (3) a specific upper difference in solubility parameter between the first and second polymers, (4) a specific upper difference in solubility parameter between the active agent and either the first or second polymer, (5) a specific upper swellability of the polymer blend, (6) a specific upper molar average solubility parameter of the polymer blend, (7) specific combinations of polymer chemical classes, and (8) the miscible polymer blend controlling the delivery of the active agent, which is not controlled by porosity in the miscible polymer blend. All of these specifically recited relationships, parameters, and functions further define a subset of combinations of polymers and active agents more specifically than in the cited combination of documents. Furthermore, with respect to dependent claims 102 and 148, there is no teaching or suggestion in the cited combination of documents that delivery of the active agent occurs predominantly under permeation control.

Appellants' system includes polymers that are miscible, focusing on a solubility parameter difference of no greater than about 3 $J^{1/2}/cm^{3/2}$. On this point of miscibility between polymers and tuning the release rates of active agents, the Examiner's attention is directed to Lyu et al., Journal of Controlled Release, 102, 679-687 (2005), in which tunable diffusion of an active agent (dexamethasone) was achieved using a miscible polymer blend, but not with an immiscible polymer blend. See, for example, Figure 9.

Once again, the relevant disclosure of Sirhan et al. for analysis of the rejections is this: Sirhan et al. identify a vast number of individual polymer species. Furthermore, the document cited as a secondary reference (Coleman et al.) does not provide that which is missing from Sirhan et al. Coleman et al. merely teach general theories about solubility parameters and predicting miscibility. Coleman et al. do not cure the deficiencies of Sirhan et al. or provide sufficient teaching or suggestion to select the combination of components recited in Appellants' claims, especially with respect to the identification of the specific combinations of polymers and

active agents according to the recited combination of at least eight relationships, parameters, and functions enumerated herein above.

Appellants submit that while the cited combination of documents describes classes of polymers that encompass at least some of the polymers from which polymers used to form the miscible polymer blends in Appellants' claims may be selected, they neither teach nor suggest the selection criteria for the recited combinations of polymers and active agents. The cited combination of documents provide no blaze marks that would direct one skilled in the art to select polymers and active agents based on their miscibility and/or the recited differences in solubility parameter.

At page 5 of the Office Action dated July 27, 2010, the Examiner acknowledged that Appellants "have provided enough written description and showed enablement since the field of polymer blends is well known" and that "there are currently no 112 1st paragraph rejections over the breadth of the claims." The Examiner alleged that "[Appellants] argue, contradictory [*sic*], that a prior art reference which is similar to their claimed invention in that it also describes numerous types of polymer blends, does not disclose their claimed blend just because numerous combinations are possible." *Id.* at 5-6 (emphasis added). Appellants earnestly disagree that the scope of the cited combination of documents is similar to the scope of the present claims. The materials recited in the present claims are described by chemistry (e.g., specific polymer chemical classes), physical properties (e.g., miscibility, relative diffusivities, difference in solubility parameters between polymers, difference in solubility parameters between the active agent and either the first or second polymer, swellability of the blend, molar average solubility parameter of the blend), and function (e.g., polymer blend controlling delivery of the active agent, which is not controlled by porosity in the polymer blend), which makes the number of combinations much smaller than that disclosed in the cited combination of documents.

The subsets of polymer and active agent combinations to which Appellants' claims are drawn is small and specific in relation to all of the possible combinations encompassed by the disclosures of the cited combination of documents and is not disclosed in the cited combination of documents. Moreover, the cited combination of documents provide no teaching or suggestion that would direct one skilled in the art to Appellants' claimed subset of polymer and active agent combinations from among the innumerable combinations described.

Appellants' position is supported by the decision of the Federal Circuit in *In re Baird*, 29 USPQ2d 1550 (1994), and, after *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007), the rationale used by the Federal Circuit in *In re Baird* was reiterated in *Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories Inc.*, 86 USPQ2d 1196 (Fed. Cir. 2008). The Federal Circuit reiterated that a claim cannot be rendered obvious by a prior disclosure that includes several unpredictable alternatives without some guidance to select features recited in the claim. The Federal Circuit contrasted a situation as presented in *KSR* (e.g., "a situation with a finite, and in the context of the art, small or easily traversed, number of options" 86 USPQ2d at 1201) with situations in which the path to the claimed subject matter is less direct. The Federal Circuit rejected the argument, based on language from *KSR*, that claims to a new drug were obvious in light of "a finite number of identified, predictable solutions." *Id.* The Federal Circuit noted that one skilled in the art, even if provided with a general class of compound from which to start, would not necessarily have chosen the starting compound selected by the patentee. *Id.*

In the present application, the combined teachings of the suggested combination of documents describe innumerable polymer species, but provide no guidance to select polymers and an active agent in relation to one another, based on the at least eight criteria recited in Appellants' claims.

Appellants' position is further supported by a recent decision of the Federal Circuit. The Federal Circuit revisited the issue of the alleged obviousness of claimed subject matter in view of

a generic disclosure that encompasses at least a portion of the claimed subject matter in *Süd-Chemie, Inc. v. Multisorb Technologies, Inc.*, 89 USPQ2d 1768 (2009). *Süd-Chemie, Inc.* involved a patent directed to a desiccant container made from a water-vapor-permeable, multilayered packaging material that included "compatible" polymeric materials, as the term "compatible" is defined in the specification of Süd-Chemie's patent. *Id.* at 1770. The patent was asserted against an alleged infringer, Multisorb, who argued that Süd-Chemie's patent was invalid as obvious over an earlier patent to Komatsu. The district court found that the polymeric materials in the Komatsu patent encompassed some of the "compatible" polymeric materials of Süd-Chemie's claims and granted summary judgment that Süd-Chemie's patent was invalid as obvious in view of the Komatsu patent. *Id.*

The Federal Circuit panel **REVERSED** the district court and critiqued the district court's analysis as follows:

> Finally, claim 1 of the '942 patent requires that the inner surfaces of the microporous and laminate films be "comprised of compatible polymeric materials." The district court concluded that Komatsu teaches the use of compatible films because "[t]he Komatsu patent suggests the employment of the same materials claimed by the '942 patent to be 'compatible polymeric materials.'" It is true that Komatsu discloses the same general classes of materials that are identified in the '942 patent. Thus, both patents state that the microporous and laminate films can be made from polyethylene, polypropylene, and other polyolefinic materials. *See* Komatsu, col. 2, ll. 19-21; col. 3, ll. 12-15; '942 patent, col. 5, ll. 12-15, 47-50. However, in concluding that Komatsu teaches the use of compatible polymeric materials, the district court failed to acknowledge that the specified classes of materials comprise a large number of substances with quite different properties, and that various combinations of those materials can be compatible or incompatible depending on how they are assembled in layers to form the container.

Id. at 1772 (emphases added).

The Federal Circuit held that the district court erred in ruling that Süd-Chemie's patent was invalid as obvious over the Komatsu patent, disagreeing with the district court "with regard to its conclusion that Komatsu teaches the same materials on the container's inner surface as those claimed in [Süd-Chemie's] patent." *Id.* at 1775.

The Federal Circuit's analysis in *Süd-Chemie* is directly applicable to the instant Application. The cited documents describe classes of polymers that may be blended, but those classes include innumerable species that have different properties, chief among those different properties are different solubility parameters. Thus, various combinations of members of the classes of polymers may possess the recited difference in solubility parameter or they may not, depending upon which members of the classes are selected.

Without guidance that directs one of ordinary skill in the art to miscible polymer blends and active agents having the recited differences in solubility parameter and the other specific relationships, the recitation of general classes of polymers and the general teaching that members of the classes may be combined does not render Appellants' claims obvious. The combinations of cited documents describe innumerable polymer species, but provide no guidance to select polymers and active agents in relation to one another and based on the criteria recited in Appellants' claims. Consequently, the obviousness analysis with respect to Appellants' claims is similar to the analysis by the Federal Circuit in these post-*KSR* cases. Appellants respectfully submit that the presently pending claims are not obvious in view of the combinations of cited documents.

Appellants note that the Examiner alleged at page 10 of the Office Action dated July 27, 2010 that "[i]t appears as though applicants are attempting to claim a well known and established scientific principle," "[e]ssentially applicants believe that the inventiveness of their claimed invention stems from the fact that like dissolves like," and "the examiner will not give patentable weight to claims directed to the well known scientific principle of mentally selecting ingredients

that will be soluble with each other." Appellants earnestly disagree with all of these allegations. Rather, as discussed herein above, Appellants have claimed methods that recite, among other things, a specific subset of combinations of polymers and active agents according to specifically recited relationships, parameters, and functions.

Review and reversal by the Board of the 35 U.S.C. §103 rejection based on Sirhan et al. in view of Coleman et al. are respectfully requested.

G. Claims 89, 91, 93-104, 134-138, 140, 141, and 143-150 are not unpatentable under 35 U.S.C. §103(a) over Hossainy et al. (U.S. Patent No. 6,153,252) in view of Van Krevelen (Properties of Polymers, 3rd ed., Chapter 7, 189-225).

There is no teaching or suggestion in each cited document of a method of tuning the delivery of an active agent from an implantable medical device to a subject using a miscible polymer blend, with the recited relationships of solubility parameters between the polymers and active agent, over a period of time, which is not controlled by porosity in the miscible polymer blend. In particular, each of the independent claims explicitly recites a combination of at least the following eight relationships, parameters, and functions that cannot be found in the cited combination of documents: (1) miscibility of the first and second polymers, (2) diffusivity of each polymer relative to each other and a target diffusivity, (3) a specific upper difference in solubility parameter between the first and second polymers, (4) a specific upper difference in solubility parameter between the active agent and either the first or second polymer, (5) a specific upper swellability of the polymer blend, (6) a specific upper molar average solubility parameter of the polymer blend, (7) specific combinations of polymer chemical classes, and (8) the miscible polymer blend controlling the delivery of the active agent, which is not controlled by porosity in the miscible polymer blend. All of these specifically recited relationships, parameters, and functions further define a subset of combinations of polymers and active agents more specifically

than in the cited combination of documents. Furthermore, with respect to dependent claims 102 and 148, there is no teaching or suggestion in the cited combination of documents that delivery of the active agent occurs predominantly under permeation control.

Appellants' system includes polymers that are miscible, focusing on a solubility parameter difference of no greater than about 3 $J^{1/2}/cm^{3/2}$. On this point of miscibility between polymers and tuning the release rates of active agents, the Examiner's attention is directed to Lyu et al., Journal of Controlled Release, 102, 679-687 (2005), in which tunable diffusion of an active agent (dexamethasone) was achieved using a miscible polymer blend, but not with an immiscible polymer blend. See, for example, Figure 9.

Once again, the relevant disclosure of Hossainy et al. for analysis of the rejections is this: Hossainy et al. identify a vast number of individual polymer species. Furthermore, the document cited as a secondary reference (Van Krevelen) does not provide that which is missing from Hossainy et al. Van Krevelen merely teaches general theories about solubility parameters and predicting miscibility. Van Krevelen does not cure the deficiencies of Hossainy et al. or provide sufficient teaching or suggestion to select the combination of components recited in Appellants' claims, especially with respect to the identification of the specific combinations of polymers and active agents according to the recited combination of at least eight relationships, parameters, and functions enumerated herein above.

Appellants submit that while the cited combination of documents describes classes of polymers that encompass at least some of the polymers from which polymers used to form the miscible polymer blends in Appellants' claims may be selected, they neither teach nor suggest the selection criteria for the recited combinations of polymers and active agents. The cited combination of documents provide no blaze marks that would direct one skilled in the art to select polymers and active agents based on their miscibility and/or the recited differences in solubility parameter.

At page 5 of the Office Action dated July 27, 2010, the Examiner acknowledged that Appellants "have provided enough written description and showed enablement since the field of polymer blends is well known" and that "there are currently no 112 1st paragraph rejections over the breadth of the claims." The Examiner alleged that "[Appellants] argue, contradictory [*sic*], that a prior art reference which is similar to their claimed invention in that it also describes numerous types of polymer blends, does not disclose their claimed blend just because numerous combinations are possible." *Id.* at 5-6 (emphasis added). Appellants earnestly disagree that the scope of the cited combination of documents is similar to the scope of the present claims. The materials recited in the present claims are described by chemistry (e.g., specific polymer chemical classes), physical properties (e.g., miscibility, relative diffusivities, difference in solubility parameters between polymers, difference in solubility parameters between the active agent and either the first or second polymer, swellability of the blend, molar average solubility parameter of the blend), and function (e.g., polymer blend controlling delivery of the active agent, which is not controlled by porosity in the polymer blend), which makes the number of combinations much smaller than that disclosed in the cited combination of documents.

The subsets of polymer and active agent combinations to which Appellants' claims are drawn is small and specific in relation to all of the possible combinations encompassed by the disclosures of the cited combination of documents and is not disclosed in the cited combination of documents. Moreover, the cited combination of documents provide no teaching or suggestion that would direct one skilled in the art to Appellants' claimed subset of polymer and active agent combinations from among the innumerable combinations described.

Appellants' position is supported by the decision of the Federal Circuit in *In re Baird*, 29 USPQ2d 1550 (1994), and, after *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007), the rationale used by the Federal Circuit in *In re Baird* was reiterated in *Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories Inc.*, 86 USPQ2d 1196 (Fed. Cir. 2008). The

Federal Circuit reiterated that a claim cannot be rendered obvious by a prior disclosure that includes several unpredictable alternatives without some guidance to select features recited in the claim. The Federal Circuit contrasted a situation as presented in *KSR* (e.g., "a situation with a finite, and in the context of the art, small or easily traversed, number of options" 86 USPQ2d at 1201) with situations in which the path to the claimed subject matter is less direct. The Federal Circuit rejected the argument, based on language from *KSR*, that claims to a new drug were obvious in light of "a finite number of identified, predictable solutions." *Id.* The Federal Circuit noted that one skilled in the art, even if provided with a general class of compound from which to start, would not necessarily have chosen the starting compound selected by the patentee. *Id.*

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The Federal Circuit panel **REVERSED** the district court and critiqued the district court's analysis as follows:

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Id. at 1772 (emphases added).

The Federal Circuit held that the district court erred in ruling that Süd-Chemie's patent was invalid as obvious over the Komatsu patent, disagreeing with the district court "with regard to its conclusion that Komatsu teaches the same materials on the container's inner surface as those claimed in [Süd-Chemie's] patent." *Id.* at 1775.

The Federal Circuit's analysis in *Süd-Chemie* is directly applicable to the instant Application. The cited documents describe classes of polymers that may be blended, but those classes include innumerable species that have different properties, chief among those different properties are different solubility parameters. Thus, various combinations of members of the classes of polymers may possess the recited difference in solubility parameter or they may not, depending upon which members of the classes are selected.

Without guidance that directs one of ordinary skill in the art to miscible polymer blends and active agents having the recited differences in solubility parameter and the other specific relationships, the recitation of general classes of polymers and the general teaching that members of the classes may be combined does not render Appellants' claims obvious. The combinations of cited documents describe innumerable polymer species, but provide no guidance to select polymers and active agents in relation to one another and based on the criteria recited in Appellants' claims. Consequently, the obviousness analysis with respect to Appellants' claims is similar to the analysis by the Federal Circuit in these post-*KSR* cases. Appellants respectfully submit that the presently pending claims are not obvious in view of the combinations of cited documents.

Appellants note that the Examiner alleged at page 10 of the Office Action dated July 27, 2010 that "[i]t appears as though applicants are attempting to claim a well known and established scientific principle," "[e]ssentially applicants believe that the inventiveness of their claimed invention stems from the fact that like dissolves like," and "the examiner will not give patentable weight to claims directed to the well known scientific principle of mentally selecting ingredients that will be soluble with each other." Appellants earnestly disagree with all of these allegations. Rather, as discussed herein above, Appellants have claimed methods that recite, among other things, a specific subset of combinations of polymers and active agents according to specifically recited relationships, parameters, and functions.

Review and reversal by the Board of the 35 U.S.C. §103 rejection based on Hossainy et al. in view of Van Krevelen are respectfully requested.

H. Claims 89, 91, 93-104, 134-138, 140, 141, and 143-150 are not unpatentable under 35 U.S.C. §103(a) over Hossainy et al. (U.S. Patent No. 6,153,252) in view of Coleman et al. (Specific Interactions and the Miscibility of Polymer Blends, Ch. 2: A Practical Guide to Polymer Miscibility, 1991; 49-156).

There is no teaching or suggestion in each cited document of a method of tuning the delivery of an active agent from an implantable medical device to a subject using a miscible polymer blend, with the recited relationships of solubility parameters between the polymers and active agent, over a period of time, which is not controlled by porosity in the miscible polymer blend. In particular, each of the independent claims explicitly recites a combination of at least the following eight relationships, parameters, and functions that cannot be found in the cited combination of documents: (1) miscibility of the first and second polymers, (2) diffusivity of each polymer relative to each other and a target diffusivity, (3) a specific upper difference in solubility parameter between the first and second polymers, (4) a specific upper difference in solubility parameter between the active agent and either the first or second polymer, (5) a specific upper swellability of the polymer blend, (6) a specific upper molar average solubility parameter of the polymer blend, (7) specific combinations of polymer chemical classes, and (8) the miscible polymer blend controlling the delivery of the active agent, which is not controlled by porosity in the miscible polymer blend. All of these specifically recited relationships, parameters, and functions further define a subset of combinations of polymers and active agents more specifically than in the cited combination of documents. Furthermore, with respect to dependent claims 102 and 148, there is no teaching or suggestion in the cited combination of documents that delivery of the active agent occurs predominantly under permeation control.

Appellants' system includes polymers that are miscible, focusing on a solubility parameter difference of no greater than about 3 $J^{1/2}/cm^{3/2}$. On this point of miscibility between polymers and tuning the release rates of active agents, the Examiner's attention is directed to Lyu

et al., Journal of Controlled Release, 102, 679-687 (2005), in which tunable diffusion of an active agent (dexamethasone) was achieved using a miscible polymer blend, but not with an immiscible polymer blend. See, for example, Figure 9.

Once again, the relevant disclosure of Hossainy et al. for analysis of the rejections is this: Hossainy et al. identify a vast number of individual polymer species. Furthermore, the document cited as a secondary reference (Coleman et al.) does not provide that which is missing from Hossainy et al. Coleman et al. merely teach general theories about solubility parameters and predicting miscibility. Coleman et al. do not cure the deficiencies of Hossainy et al. or provide sufficient teaching or suggestion to select the combination of components recited in Appellants' claims, especially with respect to the identification of the specific combinations of polymers and active agents according to the recited combination of at least eight relationships, parameters, and functions enumerated herein above.

Appellants submit that while the cited combination of documents describes classes of polymers that encompass at least some of the polymers from which polymers used to form the miscible polymer blends in Appellants' claims may be selected, they neither teach nor suggest the selection criteria for the recited combinations of polymers and active agents. The cited combination of documents provide no blaze marks that would direct one skilled in the art to select polymers and active agents based on their miscibility and/or the recited differences in solubility parameter.

At page 5 of the Office Action dated July 27, 2010, the Examiner acknowledged that Appellants "have provided enough written description and showed enablement since the field of polymer blends is well known" and that "there are currently no 112 1st paragraph rejections over the breadth of the claims." The Examiner alleged that "[Appellants] argue, contradictory [*sic*], that a prior art reference which is similar to their claimed invention in that it also describes numerous types of polymer blends, does not disclose their claimed blend just because numerous

combinations are possible." *Id.* at 5-6 (emphasis added). Appellants earnestly disagree that the scope of the cited combination of documents is similar to the scope of the present claims. The materials recited in the present claims are described by chemistry (e.g., specific polymer chemical classes), physical properties (e.g., miscibility, relative diffusivities, difference in solubility parameters between polymers, difference in solubility parameters between the active agent and either the first or second polymer, swellability of the blend, molar average solubility parameter of the blend), and function (e.g., polymer blend controlling delivery of the active agent, which is not controlled by porosity in the polymer blend), which makes the number of combinations much smaller than that disclosed in the cited combination of documents.

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I. Claims 89, 91, 93-104, 134-138, 140, 141, and 143-150 are not unpatentable under 35 U.S.C. §103(a) over Whitbourne et al. (U.S. Patent No. 6,110,483), in view of Van Krevelen (Properties of Polymers, 3rd ed., Chapter 7, 189-225).

There is no teaching or suggestion in each cited document of a method of tuning the delivery of an active agent from an implantable medical device to a subject using a miscible polymer blend, with the recited relationships of solubility parameters between the polymers and active agent, over a period of time, which is not controlled by porosity in the miscible polymer blend. In particular, each of the independent claims explicitly recites a combination of at least the following eight relationships, parameters, and functions that cannot be found in the cited combination of documents: (1) miscibility of the first and second polymers, (2) diffusivity of

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Appellants' position is further supported by a recent decision of the Federal Circuit. The Federal Circuit revisited the issue of the alleged obviousness of claimed subject matter in view of a generic disclosure that encompasses at least a portion of the claimed subject matter in *Süd-Chemie, Inc. v. Multisorb Technologies, Inc.*, 89 USPQ2d 1768 (2009). *Süd-Chemie, Inc.* involved a patent directed to a desiccant container made from a water-vapor-permeable, multilayered packaging material that included "compatible" polymeric materials, as the term "compatible" is defined in the specification of Süd-Chemie's patent. *Id.* at 1770. The patent was asserted against an alleged infringer, Multisorb, who argued that Süd-Chemie's patent was invalid as obvious over an earlier patent to Komatsu. The district court found that the polymeric materials in the Komatsu patent encompassed some of the "compatible" polymeric materials of

Süd-Chemie's claims and granted summary judgment that Süd-Chemie's patent was invalid as obvious in view of the Komatsu patent. *Id.*

The Federal Circuit panel **REVERSED** the district court and critiqued the district court's analysis as follows:

> Finally, claim 1 of the '942 patent requires that the inner surfaces of the microporous and laminate films be "comprised of compatible polymeric materials." The district court concluded that Komatsu teaches the use of compatible films because "[t]he Komatsu patent suggests the employment of the same materials claimed by the '942 patent to be 'compatible polymeric materials.'" It is true that Komatsu discloses the same general classes of materials that are identified in the '942 patent. Thus, both patents state that the microporous and laminate films can be made from polyethylene, polypropylene, and other polyolefinic materials. *See* Komatsu, col. 2, ll. 19-21; col. 3, ll. 12-15; '942 patent, col. 5, ll. 12-15, 47-50. However, in concluding that Komatsu teaches the use of compatible polymeric materials, the district court failed to acknowledge that the specified classes of materials comprise a large number of substances with quite different properties, and that various combinations of those materials can be compatible or incompatible depending on how they are assembled in layers to form the container.

Id. at 1772 (emphases added).

The Federal Circuit held that the district court erred in ruling that Süd-Chemie's patent was invalid as obvious over the Komatsu patent, disagreeing with the district court "with regard to its conclusion that Komatsu teaches the same materials on the container's inner surface as those claimed in [Süd-Chemie's] patent." *Id.* at 1775.

The Federal Circuit's analysis in *Süd-Chemie* is directly applicable to the instant Application. The cited documents describe classes of polymers that may be blended, but those classes include innumerable species that have different properties, chief among those different properties are different solubility parameters. Thus, various combinations of members of the

classes of polymers may possess the recited difference in solubility parameter or they may not, depending upon which members of the classes are selected.

Without guidance that directs one of ordinary skill in the art to miscible polymer blends and active agents having the recited differences in solubility parameter and the other specific relationships, the recitation of general classes of polymers and the general teaching that members of the classes may be combined does not render Appellants' claims obvious. The combinations of cited documents describe innumerable polymer species, but provide no guidance to select polymers and active agents in relation to one another and based on the criteria recited in Appellants' claims. Consequently, the obviousness analysis with respect to Appellants' claims is similar to the analysis by the Federal Circuit in these post-*KSR* cases. Appellants respectfully submit that the presently pending claims are not obvious in view of the combinations of cited documents.

Appellants note that the Examiner alleged at page 10 of the Office Action dated July 27, 2010 that "[i]t appears as though applicants are attempting to claim a well known and established scientific principle," "[e]ssentially applicants believe that the inventiveness of their claimed invention stems from the fact that like dissolves like," and "the examiner will not give patentable weight to claims directed to the well known scientific principle of mentally selecting ingredients that will be soluble with each other." Appellants earnestly disagree with all of these allegations. Rather, as discussed herein above, Appellants have claimed methods that recite, among other things, a specific subset of combinations of polymers and active agents according to specifically recited relationships, parameters, and functions.

Review and reversal by the Board of the 35 U.S.C. §103 rejection based on Whitbourne et al. in view of Coleman et al. are respectfully requested.

K. Claims 89, 91-97, 99, 101-103, 134-138, 140-143, 145, and 147-150 are not unpatentable under 35 U.S.C. §103(a) over Atala (U.S. Patent No. 6,576,019) in view of Van Krevelen (Properties of Polymers, 3rd ed., Chapter 7, 189-225).

There is no teaching or suggestion in each cited document of a method of tuning the delivery of an active agent from an implantable medical device to a subject using a miscible polymer blend, with the recited relationships of solubility parameters between the polymers and active agent, over a period of time, which is not controlled by porosity in the miscible polymer blend. In particular, each of the independent claims explicitly recites a combination of at least the following eight relationships, parameters, and functions that cannot be found in the cited combination of documents: (1) miscibility of the first and second polymers, (2) diffusivity of each polymer relative to each other and a target diffusivity, (3) a specific upper difference in solubility parameter between the first and second polymers, (4) a specific upper difference in solubility parameter between the active agent and either the first or second polymer, (5) a specific upper swellability of the polymer blend, (6) a specific upper molar average solubility parameter of the polymer blend, (7) specific combinations of polymer chemical classes, and (8) the miscible polymer blend controlling the delivery of the active agent, which is not controlled by porosity in the miscible polymer blend. All of these specifically recited relationships, parameters, and functions further define a subset of combinations of polymers and active agents more specifically than in the cited combination of documents. Furthermore, with respect to dependent claims 102 and 148, there is no teaching or suggestion in the cited combination of documents that delivery of the active agent occurs predominantly under permeation control.

Appellants' system includes polymers that are miscible, focusing on a solubility parameter difference of no greater than about 3 $J^{1/2}/cm^{3/2}$. On this point of miscibility between polymers and tuning the release rates of active agents, the Examiner's attention is directed to Lyu et al., Journal of Controlled Release, 102, 679-687 (2005), in which tunable diffusion of an

active agent (dexamethasone) was achieved using a miscible polymer blend, but not with an immiscible polymer blend. See, for example, Figure 9.

Once again, the relevant disclosure of Atala for analysis of the rejections is this: Atala identifies a vast number of individual polymer species. Furthermore, the document cited as a secondary reference (Van Krevelen) does not provide that which is missing from Atala. Van Krevelen merely teaches general theories about solubility parameters and predicting miscibility. Van Krevelen does not cure the deficiencies of Atala or provide sufficient teaching or suggestion to select the combination of components recited in Appellants' claims, especially with respect to the identification of the specific combinations of polymers and active agents according to the recited combination of at least eight relationships, parameters, and functions enumerated herein above.

Appellants submit that while the cited combination of documents describes classes of polymers that encompass at least some of the polymers from which polymers used to form the miscible polymer blends in Appellants' claims may be selected, they neither teach nor suggest the selection criteria for the recited combinations of polymers and active agents. The cited combination of documents provide no blaze marks that would direct one skilled in the art to select polymers and active agents based on their miscibility and/or the recited differences in solubility parameter.

At page 5 of the Office Action dated July 27, 2010, the Examiner acknowledged that Appellants "have provided enough written description and showed enablement since the field of polymer blends is well known" and that "there are currently no 112 1st paragraph rejections over the breadth of the claims." The Examiner alleged that "[Appellants] argue, contradictory [*sic*], that a prior art reference which is similar to their claimed invention in that it also describes numerous types of polymer blends, does not disclose their claimed blend just because numerous combinations are possible." *Id.* at 5-6 (emphasis added). Appellants earnestly disagree that the

scope of the cited combination of documents is similar to the scope of the present claims. The materials recited in the present claims are described by chemistry (e.g., specific polymer chemical classes), physical properties (e.g., miscibility, relative diffusivities, difference in solubility parameters between polymers, difference in solubility parameters between the active agent and either the first or second polymer, swellability of the blend, molar average solubility parameter of the blend), and function (e.g., polymer blend controlling delivery of the active agent, which is not controlled by porosity in the polymer blend), which makes the number of combinations much smaller than that disclosed in the cited combination of documents.

The subsets of polymer and active agent combinations to which Appellants' claims are drawn is small and specific in relation to all of the possible combinations encompassed by the disclosures of the cited combination of documents and is not disclosed in the cited combination of documents. Moreover, the cited combination of documents provide no teaching or suggestion that would direct one skilled in the art to Appellants' claimed subset of polymer and active agent combinations from among the innumerable combinations described.

Appellants' position is supported by the decision of the Federal Circuit in *In re Baird*, 29 USPQ2d 1550 (1994), and, after *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007), the rationale used by the Federal Circuit in *In re Baird* was reiterated in *Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories Inc.*, 86 USPQ2d 1196 (Fed. Cir. 2008). The Federal Circuit reiterated that a claim cannot be rendered obvious by a prior disclosure that includes several unpredictable alternatives without some guidance to select features recited in the claim. The Federal Circuit contrasted a situation as presented in *KSR* (e.g., "a situation with a finite, and in the context of the art, small or easily traversed, number of options" 86 USPQ2d at 1201) with situations in which the path to the claimed subject matter is less direct. The Federal Circuit rejected the argument, based on language from *KSR*, that claims to a new drug were obvious in light of "a finite number of identified, predictable solutions." *Id.* The Federal Circuit

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> the microporous and laminate films can be made from polyethylene, polypropylene, and other polyolefinic materials. *See* Komatsu, col. 2, ll. 19-21; col. 3, ll. 12-15; '942 patent, col. 5, ll. 12-15, 47-50. However, in concluding that Komatsu teaches the use of compatible polymeric materials, the district court failed to acknowledge that the specified classes of materials comprise a large number of substances with quite different properties, and that various combinations of those materials can be compatible or incompatible depending on how they are assembled in layers to form the container.

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The Federal Circuit's analysis in *Süd-Chemie* is directly applicable to the instant Application. The cited documents describe classes of polymers that may be blended, but those classes include innumerable species that have different properties, chief among those different properties are different solubility parameters. Thus, various combinations of members of the classes of polymers may possess the recited difference in solubility parameter or they may not, depending upon which members of the classes are selected.

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Review and reversal by the Board of the 35 U.S.C. §103 rejection based on Atala in view of Van Krevelen are respectfully requested.

L. Claims 89, 91-97, 99, 101-103, 134-138, 140-143, 145, and 147-150 are not unpatentable under 35 U.S.C. §103(a) over Atala (U.S. Patent No. 6,576,019) in view of Coleman et al. (Specific Interactions and the Miscibility of Polymer Blends, Ch. 2: A Practical Guide to Polymer Miscibility, 1991; 49-156).

There is no teaching or suggestion in each cited document of a method of tuning the delivery of an active agent from an implantable medical device to a subject using a miscible polymer blend, with the recited relationships of solubility parameters between the polymers and active agent, over a period of time, which is not controlled by porosity in the miscible polymer blend. In particular, each of the independent claims explicitly recites a combination of at least the following eight relationships, parameters, and functions that cannot be found in the cited

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that will be soluble with each other." Appellants earnestly disagree with all of these allegations. Rather, as discussed herein above, Appellants have claimed methods that recite, among other things, a specific subset of combinations of polymers and active agents according to specifically recited relationships, parameters, and functions.

Review and reversal by the Board of the 35 U.S.C. §103 rejection based on Atala in view of Coleman et al. are respectfully requested.

VIII. SUMMARY

For the foregoing reasons, Appellants respectfully request that the Board review and reverse the rejections of claims 89, 91-104, 134-138, and 140-150 as discussed herein and that notification of the allowance of these claims be issued.

Respectfully submitted by

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Nov. 29, 2010
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CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that this paper is being transmitted via the U.S. Patent and Trademark Office electronic filing system in accordance with 37 CFR §1.6(a)(4) to the Patent and Trademark Office addressed to the Commissioner for Patents, Mail Stop **Appeal Brief - Patents**, P.O. Box 1450, Alexandria, VA 22313-1450, on this 29th day of November 2010.

By: Dani Moore
Name: Dani Moore

CLAIMS APPENDIX

Serial No.: 10/640,853

Docket No.: P-10998.00 (134.01930101)

Claims 89, 91-104, 134-138, and 140-150 are provided below.

89. A method of tuning the delivery of an active agent from an implantable medical device to a subject at a target diffusivity, the method comprising:

receiving an implantable medical device comprising an active agent delivery system, wherein the active agent delivery system comprises an active agent and a miscible polymer blend, wherein the active agent delivery system is formed by a method comprising:

receiving a hydrophobic active agent having a molecular weight of no greater than about 1200 g/mol;

receiving a first polymer;

receiving a second polymer selected to be miscible with the first polymer to form a miscible polymer blend that controls the delivery of the active agent;

wherein at least one polymer has an active agent diffusivity higher than the target diffusivity and at least one polymer has an active agent diffusivity lower than the target diffusivity;

wherein each of the first polymer and the second miscible polymer has at least one solubility parameter, and the difference between at least one solubility parameter of each of the polymers is no greater than about 3 $J^{1/2}/cm^{3/2}$;

wherein the active agent has a solubility parameter and the difference between the solubility parameter of the active agent and at least one solubility parameter of at least one of the polymers is no greater than about 3 $J^{1/2}/cm^{3/2}$;

and further wherein each of the solubility parameters is independently determined by at least one method selected from measuring, obtaining the solubility parameter from a reference publication, taking an average of calculations performed using the Hoy Method and the Hoftyzer-van Krevelen Method, and calculating by computer simulation; and

combining the first and second polymers in amounts sufficient to form a miscible polymer blend that controls the delivery of the active agent over a period of time;

wherein:

the swellability of the miscible polymer blend is no greater than 10% by volume; and

the molar average solubility parameter of the miscible polymer blend is no greater than 25 $J^{1/2}/cm^{3/2}$;

and further wherein:

the miscible polymer blend comprises at least one hydrophobic cellulose derivative and at least one miscible polyvinyl homopolymer or copolymer selected from the group consisting of a polyvinyl alkylate homopolymer or copolymer, a polyvinyl alkyl ether homopolymer or copolymer, a polyvinyl acetal homopolymer or copolymer, and combinations thereof; or

the miscible polymer blend comprises a polyurethane and a second miscible polymer that is not a hydrophobic cellulose ester; wherein the second miscible polymer is selected from the group consisting of a polycarbonate, a polysulfone, a polyurethane, a polyphenylene oxide, a polyimide, a polyamide, a polyester, a polyether, a polyketone, a polyepoxide, a styrene-acrylonitrile copolymer, a poly(vinyl ester), a poly(vinyl ether), a polyacrylate, a poly(methyl acrylate), a polymethacrylate, a poly(methyl methacrylate), and combinations thereof; or

the miscible polymer blend comprises a poly(ethylene-co-(meth)acrylate) and a second miscible polymer not including poly(ethylene vinyl acetate); wherein the second miscible polymer is selected from the group consisting of a poly(vinyl alkylate) homopolymer or copolymer, a

poly(vinyl alkyl ether) homopolymer or copolymer, a poly(vinyl acetal) homopolymer or copolymer, a poly(alkyl and/or aryl methacrylate) homopolymer or copolymer, a poly(alkyl and/or aryl acrylate) homopolymer or copolymer, and combinations thereof; and

contacting the implantable medical device comprising the active agent delivery system with a bodily fluid, organ, or tissue of a subject to deliver the active agent over a period of time, which is not controlled by porosity in the miscible polymer blend.

91. The method of claim 89 wherein the miscible polymer blend comprises a polyurethane and a second miscible polymer that is not a hydrophobic cellulose ester; wherein the second miscible polymer is selected from the group consisting of a polycarbonate, a polysulfone, a polyurethane, a polyphenylene oxide, a polyimide, a polyamide, a polyester, a polyether, a polyketone, a polyepoxide, a styrene-acrylonitrile copolymer, a poly(vinyl ester), a poly(vinyl ether), a polyacrylate, a poly(methyl acrylate), a polymethacrylate, a poly(methyl methacrylate), and combinations thereof.

92. The method of claim 91 wherein the miscible polymer blend comprises a polyurethane and a polyphenylene oxide.

93. The method of claim 89 wherein the difference between at least one Tg of at least two of the polymers corresponds to a range of diffusivities that includes the target diffusivity.

94. The method of claim 89 wherein the active agent is incorporated within the miscible polymer blend.

95. The method of claim 89 wherein the miscible polymer blend initially provides a barrier for permeation of the active agent.

96. The method of claim 95 wherein the active agent is incorporated within an inner matrix.

97. The method of claim 89 wherein the active agent delivery system is in the form of microspheres, beads, rods, fibers, or other shaped objects.

98. The method of claim 97 wherein the critical dimension of the object is no greater than about 10,000 microns.

99. The method of claim 89 wherein the active agent delivery system is in the form of a film.

100. The method of claim 99 wherein the thickness of the film is no greater than about 1000 microns.

101. The method of claim 89 wherein the medical device is selected from the group consisting of a stent, stent graft, anastomotic connector, lead, guide wire, catheter, sensor, angioplasty balloon, wound drain, shunt, tubing, urethral insert, pellet, pump, vascular graft, valve, pacemaker, orthopedic device, replacement device for nucleus pulposus, and intraocular lens.

102. The method of claim 89 wherein delivery of the active agent occurs predominantly under permeation control.

103. The method of claim 89 wherein receiving an implantable medical device comprises making the medical device comprising;

receiving a medical device comprising a surface; and

adhering the active agent delivery system to at least a portion of the surface.

104. The method of claim 89 wherein the implantable medical device is a stent.

134. A method of tuning the delivery of an active agent from an implantable medical device to a subject at a target diffusivity, the method comprising:

receiving an implantable medical device comprising an active agent delivery system, wherein the active agent delivery system comprises an active agent and a miscible polymer blend, wherein the active agent delivery system is formed by a method comprising:

receiving a hydrophilic active agent having a molecular weight of greater than about 1200 g/mol;

receiving a first polymer;

receiving a second polymer selected to be miscible with the first polymer to form a miscible polymer blend that controls the delivery of the active agent;

wherein at least one polymer has an active agent diffusivity higher than the target diffusivity and at least one polymer has an active agent diffusivity lower than the target diffusivity;

wherein each of the first polymer and the second miscible polymer has at least one solubility parameter, and the difference between at least one solubility parameter of each of the polymers is no greater than about 3 $J^{1/2}/cm^{3/2}$;

wherein the active agent has a solubility parameter and the difference between the solubility parameter of the active agent and at least one solubility parameter of at least one of the polymers is no greater than about 3 $J^{1/2}/cm^{3/2}$;

and further wherein each of the solubility parameters is independently determined by at least one method selected from measuring, obtaining the solubility parameter from a reference publication, taking an average of calculations performed using the Hoy Method and the Hoftyzer-van Krevelen Method, and calculating by computer simulation; and

combining the first and second polymers in amounts sufficient to form a miscible polymer blend that controls the delivery of the active agent over a period of time;

wherein:

the swellability of the miscible polymer blend is greater than 10% by volume; and

the molar average solubility parameter of the miscible polymer blend is greater than 25 $J^{1/2}/cm^{3/2}$;

and further wherein:

the miscible polymer blend comprises at least one hydrophilic polymer and a second miscible polymer that is hydrophilic or hydrophobic; wherein the hydrophilic polymer is selected from the group consisting of a polyurethane, a polyvinyl alcohol, a poly(alkylene ether), a polyvinyl pyridine, a polyvinyl pyrrolidone, a polyacrylonitrile, a polyacrylamide, a polyvinyl pyrrolidone/polyvinyl acetate copolymer, a

sulfonated polystyrene, a polyvinyl pyrrolidone/polystyrene copolymer, a polysaccharide, a xanthan, a hydrophilic cellulose derivative, a hyaluronic acid, a hydrophilic polyacrylate, a hydrophilic polymethacrylate, a DNA or analog thereof, an RNA or analog thereof, heparin, a chitosan, a polyethylene imine, a polyacrylamide, an amine-containing polymer, and combinations thereof; and the hydrophobic polymer is selected from the group consisting of a polyurethane, a polycarbonate, a polysulfone, a polyphenylene oxide, a polyimide, a polyamide, a polyester, a polyether, a polyketone, a polyepoxide, a styrene-acrylonitrile copolymer, a polyvinyl alkylate, a polyvinyl alkyl ether, a polyvinyl acetal, a hydrophobic cellulose derivative, and combinations thereof; and

contacting the implantable medical device comprising the active agent delivery system with a bodily fluid, organ, or tissue of a subject to deliver the active agent over a period of time, which is not controlled by porosity in the miscible polymer blend.

135. The method of claim 134 wherein the difference between the swellabilities of at least two of the polymers corresponds to a range of diffusivities that includes the target diffusivity.

136. The method of claim 134 wherein the active agent is incorporated within the miscible polymer blend.

137. The method of claim 134 wherein the miscible polymer blend initially provides a barrier for permeation of the active agent.

138. The method of claim 137 wherein the active agent is incorporated within an inner matrix.

140. The method of claim 134 wherein the second miscible polymer is a hydrophilic polymer.

141. The method of claim 140 wherein the second miscible polymer is a hydrophilic polyurethane.

142. The method of claim 140 wherein the miscible polymer blend comprises a polyurethane and a polyphenylene oxide.

143. The method of claim 134 wherein the active agent delivery system is in the form of microspheres, beads, rods, fibers, or other shaped objects.

144. The method of claim 143 wherein the critical dimension of the object is no greater than about 10,000 microns.

145. The method of claim 134 wherein the active agent delivery system is in the form of a film.

146. The method of claim 145 wherein the thickness of the film is no greater than about 1000 microns.

147. The method of claim 134 wherein the medical device is selected from the group consisting of a stent, stent graft, anastomotic connector, lead, guide wire, catheter, sensor, angioplasty balloon, wound drain, shunt, tubing, urethral insert, pellet, pump, vascular graft, valve, pacemaker, orthopedic device, replacement device for nucleus pulposus, and intraocular lens.

148. The method of claim 134 wherein delivery of the active agent occurs predominantly under permeation control.

149. The method of claim 134 wherein receiving an implantable medical device comprises making the medical device comprising;

receiving a medical device comprising a surface; and

adhering the active agent delivery system to at least a portion of the surface.

150. The method of claim 134 wherein the implantable medical device is a stent.

EVIDENCE APPENDIX

Serial No.: 10/640,853

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None.

RELATED PROCEEDINGS APPENDIX

Serial No.: 10/640,853

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None.

CITED AUTHORITIES AND DOCUMENTS APPENDIX

Serial No.: 10/640,853

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17. 37 C.F.R. §1.113.

18. 37 C.F.R. §1.191.

19. 37 C.F.R. §41.20(b)(2).

20. 37 C.F.R. §41.37.